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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,507	06/25/2003	Boris Skurkovich	53663-5017-01	3220

28977 7590 11/03/2005

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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,507	SKURKOVICH ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 7/18/2005 is acknowledged.

In the restriction requirement mailed 6/14/05, claims 6-9 were placed in Group I and claim 10 was placed in Group II.

Applicants' amendment to claim 10 in the supplemental amendment filed 8/29/2005 is acknowledged. Applicants submit that the amendment to claim 10, which makes it a method claim depending from the method of claim 9, places claim 10 in Group I. The examiner agrees.

Therefore, claim 10 is rejoined to the claims of Group I. The restriction requirement of 6/14/05 is withdrawn.

Claims 6-10 are under consideration.

Claim Rejections - 35 USC § 112, 1st paragraph, scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering the blood levels of tumor necrosis factor-α (TNF-α) in a schizophrenic patient by intramuscular administration of anti-TNF-α antibodies, does not reasonably provide enablement for a method of treatment of schizophrenia in a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 6-10 each encompass a method of treating schizophrenia in a patient comprising administering to the patient an effective amount of an antibody to tumor necrosis factor α (TNF-α). Claim 6 is generic to any antibody, and the dependent claims recite subspecies of antibodies (claims 7, 9, and 10) or species of routes of administration (claim 8). The term "treatment" is not specifically defined in the specification, but the specification teaches that: "It is understood that treatment of a patient suffering from an early stage of other autoimmune diseases will also be particularly useful to prevent or inhibit the natural progression of the disease state to more serious stages."

The specification teaches (Example 13, pages 64-66) that a single schizophrenic individual was administered antibodies to both interferon-γ (IFNγ) and tumor necrosis factor α (TNF-α). During treatment this individual showed a reduction in the level of circulating TNF-α in the blood and improvement in seven different symptoms of schizophrenia. No other schizophrenic or healthy individuals were treated with either the antibodies or a placebo. The level of IFNγ was not measured.

While the results seen in the single treated patient are interesting, and worthy of further study, they do not enable a person of skill in the art to practice the claimed method to treat schizophrenia in a patient with TNF-α. The standard in the art for determining the effectiveness of a test compound in treating the symptoms of schizophrenia is to simultaneously conduct separate treatments with a test compound or a placebo. Without a placebo control, one of skill in the art would not know whether or not the results with the test compound are significant. Studies have shown that some schizophrenic individuals show improvement in symptoms in response to treatment with

a placebo. For example, Fenton et al, 2001 conducted a study of omega-3 fatty acid (also known as ethyl eicosapentaenoic acid, or EPA) supplementation on the symptoms of schizophrenia (Fenton et al, 2001. Am J Psychiatry. 158(12): 2071-2074). In this study 43 schizophrenic patients received EPA, and 44 patients received placebo. There was no significant difference in the improvement of the EPA treated patients and the placebo patients; that is, both groups showed equivalent levels of improvement. The authors conclude (page 2073) "The placebo response reported here is of sufficient magnitude to explain the effect of EPA in open trials". In the instant application, where the size of the treated population is one, it is unknowable whether or not the single treated patient improved due to the effect of the test compounds (said antibodies) or due to a placebo effect.

Furthermore, while a skilled artisan would predict that administration of antibodies to a cytokine would lower the circulating level of the cytokine in the blood, they would not be able to predict whether or not this would treat schizophrenia. The relevant art teaches that many studies have been conducted to measure the level of various cytokines secreted by schizophrenic patients (Hinze-Selch et al, 2001. Brain, Behavior, and Immunity 15, 282-318). These studies have not produced consistent results. Hinze-Selch teaches (pg 295) that eight studies report decreased IFN secretion, 1 reports increased IFN secretion, and 2 report no difference between patients and controls (many of these studies did not distinguish between IFNα and IFNγ). Hinze-Selch teaches (pg 295) that the one study of TNFα secretion found no difference between patients and controls. Therefore, it has not been established that overexpression of cytokine production occurs in schizophrenic patients. Even if it was established, it could be a symptom of schizophrenia and not a cause of the disease or its other symptoms. Due to the lack of a correlation between cytokine dysregulation and schizophrenic symptoms, a skilled artisan would not predict that administration of the antibodies would treat schizophrenia. Furthermore, even if enablement were to be established for treatment of the symptoms of schizophrenia, it would not establish that the method was enabled to prevent or inhibit the natural progression of the disease, which as taught in the specification, is encompassed by the claims.

Furthermore, even if the results were controlled for placebo response and were shown to be effective in treating schizophrenia, they would not provide enablement for treatment with anti-TNF-α antibodies alone; because two antibodies were administered simultaneously one of skill in the art would not be able to determine whether or not administration of a single antibody would have the same effect. A skilled artisan would need to engage in undue experimentation to test the administration of a single antibody (to TNF-α) in schizophrenic patients to determine whether it was effective in treatment.

It is acknowledged that the level of skill of those in the art is high, but it is not disclosed and not predictable from the limited teachings of the relevant art and specification whether or not the method of the present invention could be used to treat schizophrenia. There is a single example of administration of antibodies to a person with schizophrenia, which does not meet the standard in the art for validating whether or not a treatment is effective. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use the method for treatment of schizophrenia. Thus the specification fails to teach the skilled artisan how to use the method for treatment of schizophrenia without resorting to undue experimentation. To practice the claimed invention to treat schizophrenia, a skilled artisan would first need to engage in undue experimentation test populations of schizophrenic patients simultaneously with the test compound or placebo to determine if administration of the antibodies is effective.

Claim 7 also lacks enablement because a skilled artisan would not know how to make and use "a biologically active fragment", or species or allelic variant, of a polyclonal, monoclonal, humanized, or synthetic antibody of the invention. The specification teaches, "The term "biologically active fragment" is intended to mean a part of the complete molecule which retains all or some of the catalytic or biological activity possessed by the complete molecule, especially activity that allows specific binding of the antibody to an antigenic determinant." The specification further teaches, "A "variant" or "allelic or species variant" of a protein refers to a molecule substantially similar in structure and biological activity to the protein. Thus, if two molecules possess a common activity and may substitute for each other, it is intended that they are

"variants," even if the composition or secondary, tertiary, or quaternary structure of one of the molecules is not identical to that found in the other, or if the amino acid or nucleotide sequence is not identical." The specification does not provide any examples of making or using a biologically active fragment, or species variant or allelic variant, of the invention.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs that provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity that is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of an antibody resulted in the loss of antigen-binding function. It is unlikely that fragments and variants antibodies as encompassed by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions of the antibodies in unspecified order and/or fused to any human or nonhuman framework sequence, have the required binding function. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

The claims encompass the following routes of administration of administered anti-TNFα: intramuscularly, intravenously, intradermally, cutaneously, ionophoretically,

topically, locally and inhalation. The specification teaches in example 13 that TNFα and IFNγ were administered intramuscularly (see page 65, line 2), which resulted in a drop in TNFα levels. The specification does not provide any examples of administration by other routes, and it is not predictable whether or not other administration routes would result in a decrease in TNFα levels. Overall, the relevant literature reports that the goal of delivering proteins and peptides non-invasively has only achieved modest success, with poor applicability to proteins and peptides (see pg 343, col 1-2 of Pettit et al. 1998. Trends Biotechnol. 16: 343-349.) The problems posed by proteins and peptides are their large molecular size, electrical charge, relatively hydrophilic nature, and relative instability in environments of extreme pH or proteolytic activity (such as the stomach and intestine) (pg 343, col 2). Pettit reviews several routes of protein administration and the limitations that have been encountered. For example, limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (pg 344-345). Direct injection of protein or peptide drugs into the brain is undesirable because diffusion of these molecules is poor in parachymal brain tissue (pg 346, col 2). The delivery of proteins and peptides to the surface of the eye is complicated by normal process of blinking, tearing, and drainage form the eye (pg 346, col 2). Although much effort has been given to the transdermal delivery of pharmaceutical products, clinical applications have been limited to non-protein drugs because of the skin's poor permeability to proteins and peptides (pg 343, col 2). Additionally, proteins or peptides administered systemically must resist clearance via molecular filtration by the kidney and clearance by the reticuloendothelial system (pg 345, col 2). Therefore, the state of the prior art establishes the unpredictability of delivering proteins to a subject. Therefore one of skill in the art would need to engage in undue experimentation to determine whether or not other modes of administration would result in a decrease in TNFα.

Due to the large quantity of experimentation necessary to determine if the method could be used to treat schizophrenia as well as produce biologically active fragments or variants, whether or not routes of administration other than intramuscular

would result in a decrease in TNFα, the lack of direction/guidance presented in the specification regarding same, lack of a significant study size in the example given and lack of examples of biologically active fragments or variants, and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention. What Applicant has provided is a mere wish or plan and an invitation to experiment to determine whether or not the method of treatment with antibodies to TNF-α would actually work to treatment schizophrenia.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claim 7, there is a lack of adequate written description for each of the following genera of antibodies: a biologically active fragments or variants (allelic or species) of a polyclonal antibody, monoclonal antibody, humanized antibody, and synthetic antibody. The instant disclosure of antibodies to TNF-α does not adequately support the scope of each claimed genus. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). With the exception of each antibody expressed by a disclosed hybridoma cell line, the skilled artisan cannot envision encompassed variants that fall within a genus composed of antibodies that are biologically active fragments of the antibodies to TNF-α. Although one of skill in the art would reasonably predict that other antibodies exist that would be included in each genus, one would not be able make useful predictions as to the identity of these antibodies based on the information disclosed in the specification. The information disclosed in the specification does not include information on what constitutes a biological active fragment of one of these antibodies, what constitutes a species or allelic variant of one of these antibodies, the sequence of any of these

antibodies, or which amino acids can be altered within these antibodies and still retain biological activity. As summarized above, Rudikoff et al, 1982 (cited above) teaches that the alteration of a single amino acid in the CDR of an antibody can result in the loss of antigen-binding function. Therefore, only the antibodies to TNF-α but not the full breadth of the claims, meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite because it is unclear whether "a patient" referred to in line 1, is a patient who already has "schizophrenia", or whether the term encompasses any patient. Therefore, this claim is being broadly interpreted to encompass any patient.

The term "effective" in claim 6 is a relative term which renders the claim indefinite. The term "effective" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term effective renders indefinite the amount of an antibody to be administered.

Claims 7-10 are rejected for depending from indefinite claim 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-9 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Skurkovich et al, U.S. Patent No. 5,888,511, published 3/30/1999 (cited on the IDS submitted 4/19/2004 by Applicants).

Claim 6 encompasses a method comprising administering to a patient with schizophrenia an effective amount of an antibody to tumor necrosis factor α (TNF-α).

Skurkovich teaches (col 4, lines 51-54) a method comprising administering to a patient with an autoimmune disease an effective amount of anti-TNF antibodies. Skurkovich further teaches (col 12, line 49) that the genus of autoimmune diseases includes schizophrenia. The specification further teaches (col 2, line 44) that TNF includes TNFα or TNFβ, and provides examples (see Examples 4 and 5) wherein anti-TNFα antibodies are used to treat autoimmune diseases. Therefore, Skurkovich clearly anticipates instant claim 6.

Claims 7 and 9 each encompass the method of claim 6 wherein the administered antibody is a polyclonal or monoclonal antibody.

Skurkovich teaches (col 15, lines 2-8) "As used herein, the term "antibody" is intended to include monoclonal or polyclonal antibodies, or a combination thereof, humanized forms of the monoclonal antibodies (comprising only human antibody protein), and chimeric monoclonal antibodies, as well as biologically active fragments, functional equivalents, derivatives, or allelic or species variants thereof." Therefore, the method of treatment of schizophrenia by administering antibodies taught by Skurkovich includes polyclonal or monoclonal antibodies and clearly anticipates claims 7 and 9.

Claim 8 encompasses the method of claim 6 wherein the antibody is administered by various routes, e.g. intramuscularly or intravenously.

Skurkovich teaches (col 18, lines 21-23) that the "autoimmune inhibitors can be administered by inhalation, orally, subcutaneously, intramuscularly, intravenously, transdermally, intranasally, rectally, and the like." Therefore, the method of treatment of

schizophrenia by administering antibodies taught by Skurkovich includes intramuscular or intravenous administration and clearly anticipates claim 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Skurkovich et al, U.S. Patent No. 5,888,511, published 3/30/1999 (cited on the IDS submitted 4/19/2004 by Applicants) as applied to claims 6-9 above, and further in view of Spinelli et al, 2000. Biochemistry. 39(6): 1217-22.

Claim 10 encompasses a method of claim 6 wherein the antibody is a heavy chain antibody selected from the group consisting of a camelid antibody, a heavy chain disease antibody, or a variable heavy chain immunoglobulin. The teachings of Skurkovich are summarized above. Skurkovich further teaches that functional equivalents of antibodies can be used in the method of treatment ""Functional equivalents" of an antibody include any molecule capable of specifically binding to the same antigenic determinant as the antibody, thereby neutralizing the molecule, e.g., antibody-like molecules, such as single chain antigen binding molecules." Skurkovich does not teach using a heavy chain antibody, such as camelid antibodies, in the method of treatment.

Spinelli et al teaches the generation of camelid antibodies and the advantages of camelid antibodies, such as "their levels of expression and solubility are significantly higher than those of classical Fab or Fvs."

It would be obvious to the person of ordinary skill in the art at the time the invention was made to use a camelid antibody as taught by Spinelli in the method of

treatment taught by Skurkovich. The person of ordinary skill in the art would be motivated to do so because, in the absence of other evidence, a camelid antibody would work as well as any other antibody to interact with the cytokines, and would confer the advantages of higher levels of expression and solubility. The person of ordinary skill in the art would have expected success because Skurkovich teaches that functionally equivalent antibodies can be used in the method.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 10/422119. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Instant claim 6 is drawn to a method of treatment of schizophrenia comprising administration of antibody to TNFα. Claim 1 of '119 is drawn to a method of treatment of schizophrenia comprising administration of an antibody to TNFα and an antibody to IFNγ. As stated in the MPEP 2111.03 [R-2] (Transitional Phrases): "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps." Therefore, the method of claim 1 of '119 is a species that is fully

encompassed by the method of instant claim 6. For this reason, claim 1 of '119 anticipates instant claim 6. Instant claims 7-10 depend from instant claim 6 and recite identical limitations as claims 2-5 of '119, which depend from claim 1 of '119. Therefore, claims 2-5 of '119 anticipate instant claims 7-10.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Bridget E. Bunner

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PATENT EXAMINER